

신 허혈 재관류 백서 모델에서 sildenafil의 신보호 효과

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Pretreatment of Sildenafil Attenuates Ischemia-Reperfusion Renal Injury

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Introduction : Sildenafil (Viagra; Pfizer, New York, NY) is the first commercially available selective inhibitor of phosphodiesterase- 5 (PDE5) to be widely used for the treatment of erectile dysfunction. In recent years, there has been considerable interest in investigating the role of sildenafil in protection against injury of heart in animal models. We evaluated the protective effect of sildenafil against experimental renal IR injury.

Methods : Male SD rats were divided into seven groups; sham operative rats, sildenafil- sham rats (0.5 mg/kg, intraperitoneal (IP) dose), L- NAME- sham rats (15 mg/kg, intraperitoneal (IP) dose), untreated IR rats (reperfusion 35 minutes after nephrectomy of right kidney with clamping of left renal artery and vein) and Sildenafil-treated IR rats (0.5 mg/kg, single IP dose 30 min prior to IR injury). L- NAME- treated IR rats, and Sildenafil and L- NAME- treated IR rats. Renal gene expression levels of TNF- α , Fas, FasL, Bcl- 2, and GAPDH were measured by real- time PCR 24 hrs after IR injury. Renal bcl- 2, caspase- 3 activation was evaluated by western blot, We examined TUNEL, and light microscopic findings.

Results : Serum level of creatinine in etanercept treated IR rats 24 hrs after IR injury (1.24 ± 0.36 mg/dL, $M \pm SD$) was significantly lower than that of untreated IR injured rats (2.20 ± 0.52 mg/dL, $M \pm SD$) ($p < 0.01$). Renal gene expression levels of TNF- α , Fas and FasL in untreated IR rats were significantly higher than those of Sham op rats. The levels of TNF- α , Fas and FasL gene expressions of sildenafil treated IR rats were significantly lower than those of untreated IR rats (all, $p < 0.01$). The Bcl- 2 gene expression level of sildenafil treated IR rats was significantly higher than that of untreated rats ($p < 0.05$). Pretreatment of sildenafil in IR injured rats significantly reduced renal caspase- 3 activation ($p < 0.01$) and TUNEL positive apoptotic cells ($p < 0.01$), and significantly increased bcl- 2 protein.

Conclusion : In conclusion, the results of the present study suggest that sildenafil has protective effect on experimental IR renal injury via anti- apoptotic effect.

Key Words : 실데나필, 허혈재관류, 세포사멸

Sildenafil, Ischemia reperfusion, Apoptosis